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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,400	10/30/2003	William D. Huse	X16755D	7475

25885 7590 09/27/2006

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 09/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/697,400	HUSE ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2003*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *25-42* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 25-36, drawn to a heteromeric variable region having higher antigen binding affinity than a donor heteromeric variable region, classified in class 530, subclass 387.3.

II. Claims 37-38, drawn to a method of expressing a heteromeric variable region having higher antigen binding affinity than a donor heteromeric variable region comprising three light chain donor CDRs and three heavy chain donor CDRs, wherein the method comprises providing a first oligonucleotide encoding an altered light chain variable region and a second oligonucleotide encoding an altered heavy chain variable region, expressing said first and second oligonucleotides under conditions such that the heteromeric variable region having a higher antigen binding affinity is generated, classified in class 435, subclass 69.1.

III. Claims 39-42, drawn to a method of expressing a heteromeric variable region having higher antigen binding affinity than a donor heteromeric variable region comprising three light chain donor CDRs and three heavy chain donor CDRs, wherein the method comprises providing a first oligonucleotides encoding four unvaried human germline light chain framework regions, a population of second oligonucleotides encoding donor light chain CDR variants, third oligonucleotides encoding four

unvaried human germline heavy chain framework regions and a population of fourth oligonucleotides encoding donor heavy chain CDR variants, mixing said first oligonucleotides and said population of second oligonucleotides such that a population of fifth oligonucleotides encoding light chain variable regions is generated and mixing said third oligonucleotides and said population of fourth oligonucleotides such that a population of sixth oligonucleotides encoding heavy chain variable regions is generated, expressing said fifth and sixth populations of oligonucleotides to produce combinations of heteromeric variable region binding fragments, classified in class 435, subclass 69.6.

2. The inventions are distinct, each from the other because of the following reasons:

The methods of Inventions of Groups II-III differ in the method steps, parameters and in the reagents used. Invention II recites a method of expressing a heteromeric variable region having higher antigen binding affinity than a donor heteromeric variable region comprising three light chain donor CDRs and three heavy chain donor CDRs, wherein the method comprises providing a first oligonucleotide encoding an altered light chain variable region and a second oligonucleotide encoding an altered heavy chain variable region, expressing said first and second oligonucleotides under conditions such that the heteromeric variable region having a higher antigen binding affinity is generated; Invention III recites a method of expressing a heteromeric variable region having higher antigen binding affinity than a donor heteromeric variable region

comprising three light chain donor CDRs and three heavy chain donor CDRs, wherein the method comprises providing first oligonucleotides encoding four unvaried human germline light chain framework regions, a population of second oligonucleotides encoding donor light chain CDR variants, third oligonucleotides encoding four unvaried human germline heavy chain framework regions and a population of fourth oligonucleotides encoding donor heavy chain CDR variants, mixing said first oligonucleotides and said population of second oligonucleotides such that a population of fifth oligonucleotides encoding light chain variable regions is generated and mixing said third oligonucleotides and said population of fourth oligonucleotides such that a population of sixth oligonucleotides encoding heavy chain variable regions is generated, expressing said fifth and sixth populations of oligonucleotides to produce combinations of heteromeric variable region binding fragments. The examination of all groups would require different searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues. Thus, inventions II-III are separate and distinct in having different method steps, parameters and reagents used and are patentably distinct.

Inventions II and III are directed to related processes. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the invention of Group III recites separate populations of oligonucleotides encoding the

frameworks and CDRs for each of the heavy and light chain variable regions (i.e., four different populations of oligonucleotides), wherein the first and second populations of oligonucleotides are mixed to produce a fifth population of oligonucleotides encoding the light chain variable regions and wherein the third and fourth populations of oligonucleotides are mixed to produce a sixth population of oligonucleotides encoding the heavy chain variable regions and expressing the fifth and sixth populations of oligonucleotides to produce the heteromeric variable region, which has a materially different design than the process of Group II, i.e., is mutually exclusive. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

Inventions II and I are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the heteromeric variable region of Group I can be made by the materially different process of Group III, which differs in the method steps, parameters and reagents used from the method of Group II.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter and different classifications, restriction for examination purposes as indicated is proper.

4. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain

dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder.

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827